REMARKS

Claims 1-16 and 27-32 remain in the application for further prosecution. Claims 17-26 were withdrawn from consideration as the result of an election of Claims 1-16 without traverse.

In order to advance prosecution and place the claims in condition for appeal, Claims 1, 2, 9, and 27 would be amended to more completely describe the wells in which microstructures are located. Claim 27 also has been amended to correct an informality noted by the Examiner.

Claims 1, 5-9 and 13-16 were rejected under 35 U.S.C. 103(a) as unpatentable (i.e. obvious) over Columbus (U.S. 4,233,029) in view of Przybylowicz et al (U.S. 3,992,158) (Przybylowicz). Both references could be relevant to the present invention only by giving Claims 1 and 9 a very broad reading beyond the usage of one skilled in the art. While it may be the rule that the PTO will give a broad reading to the claims, the rule is limited by requiring that the claims be given their ordinary meaning as understood by one skilled in the art. The question then, is how would one skilled in the art interpret the present claims?

The Applicant's invention relates to the problem of distributing liquid samples over reagents disposed on substrates, which are positioned in wells of microfluidic devices. As discussed in paragraphs 0040-0044 of the published application U.S. 2004/0265171 A1 (or page 9, line 20 to page 11, line 19), it is important that the sample is uniformly distributed over the reagents if accurate results are to be obtained. In many cases, the substrates act as capillaries and draw the sample into the substrate. Another problem related to distributing the sample liquid over the reagents is the interference of air bubbles that are not purged from the microfluidic well. Again, the use of microstructures such as those described in the published application at paragraphs 0046-0049 (or page 11, line 21 to page 12, line 25) have been found to assist in uniformly distributing the liquid sample over the reagents immobilized on substrates and in

purging air from the microfluidic well. A preferred embodiment described in Figs. 3 and 4 is the subject of Claims 27-32.

Turning to Columbus, it is evident from his Fig. 1 that if a liquid sample enters opening 26 that the liquid will flow in all four possible directions. Columbus describes movement of liquid along the grooves 44 and the jumping of liquid over the peaks of the grooves until, depending on the amount of liquid present, the entire device 10 is filled. It appears that Columbus intended to provide controlled distribution of the liquid at a uniform rate along all the edges (see column 10, lines 1-6). In a preferred use, the liquid leaves the device and proceeds to a test site where it contacts an electrode (see column 10, lines 7-10, Figs. 9-11). Various types of downstream processing were suggested, see column 9, lines 50-68, but the uniform distribution of the liquid over reagents immobilized on substrates in microfluidic wells was not disclosed or suggested.

The following analysis of Claim 1, as it would be amended in the proposed amendment, will compare the Applicant's microfluidic device with that of Columbus.

Claim 1	Columbus
A microfluidic device for assaying a liquid biological sample of 10 μL or less.	o Columbus also maybe considered a microfluidic device, although it uses drop volumes between 5 and 1,000μL (column 4, lines 45-47), which will relate to the purpose of the Columbus device. Columbus spreads his sample over the space between two surfaces, rather than filling a well containing a substrate. One would expect that Columbus would employ liquid volumes significantly greater than 10 μL, not less than 10 μL.

said device including at least one well in which a reagent or conditioning agent is immobilized on a substrate placed in said well.	o Columbus has no well containing a reagent or conditioning agent immobilized on a substrate placed in a well. Instead, reliance is placed on a reagent in Przybylowicz, which relates to composites that direct a sample liquid to a reagent layer. Columbus employs surfaces that are 60 to 600 μm apart (column 11, lines 57-59) to create capillary forces that spread the sample liquid along and over the grooves cut into the surfaces. (The Applicant's wells typically are deep enough so that liquids entering from a capillary would spread irregularly unless directed by the microstructures of the invention.) Columbus merely suggests that a reagent could be disposed on the surface of his V-shaped grooves, which are not wells. As such, Columbus cannot be read to suggest that uniform contact of a sample liquid with a reagent would be obtained.
said well having an entry at a side thereof from a capillary passageway.	o Columbus illustrates an entry to his pair of surfaces from the middle of one of them. The liquid thus spreads in 360° to reach the outer edges of the surfaces. (Entering a well from one side, the well having no ability to distribute a liquid by capillary forces, causes the liquid to proceed in a generally unidirectional manner.). Columbus's entry also is not from a capillary passageway.
the improvement comprising a microstructure disposed in said well for directing said sample from the entry of said well over said substrate containing said reagent or conditioning agent.	o Columbus directs a liquid sample in all directions from a center entry. Therefore, if only a portion of the grooved surface contains a reagent, a uniform application of the liquid to the reagent would not be possible. Alternatively, if all the grooved surface contains reagent, then the movement of liquid is not unidirectional.
in a predetermined uniform manner and purging air from said well.	o Columbus purges air from between his surfaces by orientation of the two sets of grooves (column 6, lines 13-20), which is said to be critical. The Applicant's device moves liquid in a one directional manner because the liquid enters from one side of the well opposite the vent opening.

As the Examiner noted, Columbus suggested that reagents could be disposed on the grooved surfaces, but there is no suggestion that the reagents are immobilized on substrates, as in the Applicant's invention. The reference in Columbus to U.S. 3,992,158, Przybylowicz, cited also by the Examiner, is unclear since the '158 patent concerns multilayer analytical device that features an "isotropically porous spreading layer comprising a non-fibrous material" (Claim 1) that is intended to provide a uniform concentration of the sample to the reagent layer (column 3, lines 30-33). Such a spreading layer should not be equated with the microstructures of the present application. At column 14, beginning at line 34, a typical application of the '158 multilayer device is described. It is obvious that the multi-layer device of the "158 patent is intended for use in an instrument that detects the results of contacting a sample with the reagents. The use of such multi-layered element on the surfaces of Columbus does not correspond to the Applicant's use of microstructures to assure that a liquid sample is uniformly distributed over reagents. Applying the multi-layers of the '158 patent would rely on the "porous spreading layer" to distribute liquid, rather than the microstructures described in the present application.

Regarding Claim 5, the Examiner considers the grooved surface 18 to be a substrate. However, in the context of the present invention a "substrate" is a solid material on which the reagent or conditioning agent has been deposited (paragraph 0046 or page 11, line 30 to page 12, line 2). Typically, such substrates are fibrous pads. Thus, the substrates of the Applicant's application are applied to a well in a microfluidic device. The surface of the well itself is not the substrate. As mentioned above, it is the nature of the substrates that makes it necessary to provide microstructures to assure uniform sample distribution.

Regarding Claim 6, the Examiner again relates grooves 18 of the Columbus device with the Applicant's substrate. Again, as explained above, Columbus's grooves 18 are not the Applicant's substrate.

Regarding Claim 7, the Examiner relates the truncated ridges 46 of Columbus (Fig. 7a) to a ramp. Since a "ramp" is typically defined as an inclined surface, relating the flat ends of a series of grooves to a ramp is not a reasonable interpretation of Columbus.

Regarding Claims 9 and 13-16, the Examiner contends that Columbus teaches all of the Applicant's apparatus structure. However, it should be evident to one skilled in the art that the Columbus device of Fig. 1 and the Applicant's microfluidic devices, shown generally in Figs. 1 and 2 and more specifically the introduction of a liquid sample into the well of a microfludic device in Figs. 3 and 4, are clearly not alike, nor would they function in the same way. Reconsideration is requested.

Claims 2-4, 10-12, and 27-32 were rejected under 35 U.S.C. 103(a) as unpatentable over Columbus in view of Przybylowicz '158 and further in view of Peters (U.S. 6,296,126 B1). The deficiencies of Columbus and Przybylowicz have been discussed above. Peters is a co-inventor in the present application and his patent was cited in paragraph 0014 of the published application. (or page 4, lines 2-5). If, as the Applicant's contend, independent Claims 1 and 9 are patentable, then Claims 2-4 and 10-12 should also be patentable. Although Peters does show posts having wedge-shaped cutouts, he does not suggest the use which the present invention discloses. In Peters, the wedge-shaped cutouts serve as channels to direct the flow of liquids. The Applicant's posts may include wedge-shaped cutouts, but they are positioned at right angles to the direction in which liquid flows.

Peters was concerned with emptying capillaries into a collecting chamber (see Claim 1). Even in the embodiment of Figs. 7-8, where a row of posts are used, their function is to remove liquid from membrane 32, which then flows via wedge-shaped cutouts to second chamber 27 and then into the third chamber 29. Thus, the posts do not distribute a liquid sample uniformly over reagents on a substrate by passing the liquid through spaces between them. Therefore, even if Columbus and Przybylowicz are assumed to make independent Claims 1 and 9 obvious, Peters is not sufficient to make Claims 2-4, 10-12, and 27-32 obvious and unpatentable.

The Examiner is urged to enter the proposed amendments, reconsider, and withdraw his rejections. If further amendment is considered necessary, the Examiner is invited to contact the Applicant's attorney at the telephone number provided below.

The Commissioner is hereby authorized to charge deposit Account No. 10-0447 (55197-00010USPT) for any fees inadvertently omitted which may be necessary now or during the pendency of this application, except for the issue fee.

Respectfully submitted,

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Date

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